REMARKS

I. Formal matters

Claims 27-43 are currently pending in this application. No claims are amended, canceled or added. Reconsideration and withdrawal of all rejections in view of the following remarks are respectfully requested.

II. Rejections under 35 U.S.C. § 102 are overcome

Claims 27-29 and 31-36 were rejected under 35 U.S.C. §102(b) as allegedly being anticipated by U.S. Patent No. 5,565,324 to Still et al. ("STILL"). The Office Action contends that:

> Still et al. teach a system where cells (biological sensor material) may be embedded substantially homogeneously in a gel which may be polyacrylamide, agarose, gelatin, etc. (diffusion controlling matrix) (column 31, line 62-column 32, line 6). One could further place a grid over the gel defining areas of one or no particle (column 32, lines 6-15). Still et al. further discloses assays where one could release product, incubate for a sufficient time, followed by spreading a vital dye over the gel, so that cells which absorbed the dye or did not absorb the dye could then be distinguished (means for detecting spatial distribution) (column 32, lines 10-15). By employing recombinant techniques, the cells can be designed such that binding to a surface membrane protein will result in an observable signal, such as a fluorescent product (bioluminescent cells) (column 30, lines 35-45).

See Office Action, page 2. Applicants respectfully disagree with this rejection and traverse as follows.

Applicants respectfully assert that the present rejection impermissibly combines features of distinct embodiments, none of which, when taken alone, teach each and every element of the claimed invention. As will be appreciated by the Office, the M.P.E.P § 2131 states that "[a] claim is anticipated only if **each and every** element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *See Verdegaal Bros. V. Union Oil Co. of California*, 814 F.2d 628, 631 (Fed. Cir. 1987) (emphasis added). However, the case

law additionally requires that "[t]o anticipate, every element and limitation of the claimed invention must be found in a single prior art reference, **arranged as in the claim**." *Brown v. 3M*, 265 F.3d 1349, 1351, 60 USPQ2d 1375 (Fed. Cir. 2001), *cert. denied*, 122 S. Ct. 1436 (2002) (emphasis added). Further, "the reference ... must clearly and unequivocally disclose the claimed compound or direct those skilled in the art to the compound **without any need for picking, choosing, and combining various disclosures** not directly related to each other by the teachings of the cited reference." *In re* Arkley, 455 F.2d 586, 587, 172 USPQ 524 (CCPA 1972). "Unless all the elements are found in a single piece of prior art in exactly the same situation and united the same way to perform the identical function, there is no anticipation." *Sandisk Corp. v. Lexar Media, Inc.*, 91 F. Supp.2d 1327, 1336 (N.D. Calif. 2000) (emphasis added). In other words, "[n]ot only must a prior patent or publication contain all of the claimed elements of the patent claim being challenged, but they **'must be arranged as in the patented device**.' " *Aero Industries Inc. v. John Donovan Enterprises-Florida Inc.*, 53 USPQ2d 1547, 1555 (S.D. Ind. 1999) (emphasis added).

The presently claimed invention is directed to a system for obtaining a spatially-resolved image of signals indicative of the presence of at least one substance, comprising (a) a sheet of diffusion-controlling matrix of dimensions sufficient to permit bringing material to be detected into contact with at least one spatially-discrete area of said sheet, said matrix being selected from the group consisting of secondary valence gels, synthetic polymer gels and viscous solutions; (b) at least one biological sensor material suspended throughout said sheet of diffusion-controlling matrix and capable of producing at least one signal in response to the presence of at least one substance which is in contact with at least one spatially-discrete area of said sheet of diffusion-controlling matrix, said at least one biological sensor material being bioluminescent cells with reporter gene constructs, and (c) means for detecting the spatial distribution, relative to said sheet of diffusion-controlling matrix, of signal(s) produced in said sheet of diffusion-controlling matrix by said biological sensor material when said at least one substance is in contact with at least one spatially-discrete area of said sheet of diffusion-controlling matrix.

STILL generally relates to a method for carrying out combinatorial chemistry for synthesizing libraries of compounds on solid particles. The combinatorial chemistry is carried out in a manner such that sequential synthetic schemes can be recorded using organic 'tag' molecules, which can be analyzed to determine the reaction history (e.g. reagents used, stages etc.). The particles carrying the library products can be screened for compounds with characteristics of interest. See STILL, Summary of the Invention, column 3, lines 5-45.

It is respectfully asserted that, in order to allegedly meet the requirements of the presently claimed invention, the instant Office Action impermissibly picks, chooses, and combines various disclosures of STILL, none of which contain all of the claimed elements as arranged in the claimed invention.

The Office Action first cites to column 31, line 62-column 32, line 6 for the alleged teaching of "a system where cells (biological sensor material) may be embedded substantially homogenously in a gel which may be polyacrylamide, agarose, gelatin, etc. (diffusion controlling matrix)." More in particular, the cited section describes an assay scheme involving gels whereby the "molecule or system, e.g. cell, to be acted upon" is embedded homogenously in the gel. The section further describes spreading particles of interest over the gel. It is further described that desired products having hydrolytic activity can be detected by adding a hydrolysable substrate to the gel which upon hydrolysis would emit fluorescence. The section then describes mechanically selecting the particles associated with the fluorescent signals. It is respectfully submitted that the embodiment described at column 31, line 62-column 32, line 6 does not contain all of the claimed elements of the presently rejected claim. More specifically, the cited section of STILL fails to describe a sheet of diffusion-controlling matrix comprising a biological sensor material formed from bioluminescent cells with reporter gene constructs. The cited section additionally does not describe any means for detecting the spatial distribution of signal(s) produced by the biological sensor material.

The Office Action then cites to column 32, lines 6-15, for the alleged teaching of a grid placed over the gel and column 32, lines 10-15 for the alleged teaching of "assays where one could release the product, incubate for a sufficient time, followed by spreading a vital dye over

the gel, so that cells which absorb the dye or did not absorb the dye could then be distinguished (means for detecting spatial distribution)". This cited section refers to yet another assay embodiment wherein the cells to be acted upon are spread out over the gel to create a cellular lawn. It further refers to spreading out the particles of interest and placing a grid over the gel. The section also describes that for cytotoxic compounds, the compounds are released from the beads and incubated for a period of time after which a vital dye can be spread over the gel to distinguish viable and nonviable cells. In this embodiment, the cells are not emitting a signal in response to the desired product, but rather, it is the presence of dead cells in the vicinity of the particles having a cytotoxic "desired product" that identifies particles of potential interest. It is respectfully submitted that the embodiment described at column 32, lines 6-15 does not contain all of the claimed elements of the presently rejected claim. More specifically, the cited section of STILL fails to describe a sheet of diffusion-controlling matrix comprising a biological sensor material formed from bioluminescent cells with reporter gene constructs. The cited section additionally does not describe any means for detecting the spatial distribution of signal(s) produced by the biological sensor material.

Lastly, the Office Action cites to column 30, lines 35-45 for allegedly teaching recombinant techniques for modifying cells such "that binding to a surface membrane protein will result in an observable signal, such as a fluorescent product (bioluminescent cells)." This cited section of STILL describes a two-stage screening assay which "uses binding as an initial screen, followed by biological activity with a viable cell in a second screen." The embodiment further describes sorting the cells (which are physically associated with a particular particle) using a FACS to identify particles of interest. The cells of this embodiment are engineered to express an enzyme capable of transforming a leuco dye to a colored or fluorescent product. This cited section of STILL fails to describe a sheet of diffusion-controlling matrix comprising a biological sensor material formed from bioluminescent cells with reporter gene constructs. It is respectfully submitted that the embodiment described at column 30, lines 35-45 does not contain all of the claimed elements of the presently rejected claim. More specifically, the cited section of STILL fails to describe a sheet of diffusion-controlling matrix comprising a biological sensor

material formed from bioluminescent cells with reporter gene constructs. The cited section additionally does not describe any means for detecting the spatial distribution of signal(s) produced by the biological sensor material. While the FACS device may detect cells of interest, it does so by sorting the cells in a linearized manner, i.e. probing one cell at a time as each passes through the FACS laser beam detector. Such an approach is not capable of detecting the spatial distribution of the signals of the biological sensor material.

As shown above, the Office Action does not point to a single teaching or embodiment in STILLS which meets each and every element of the claimed invention, and which is presented and arranged in accordance with the elements of the claims. Instead, it attempts to string together many independent teachings found in completely separate embodiments in order to allege an anticipation by STILLS. This approach is inconsistent with the Federal Circuit's view that "to anticipate, every element and limitation of the claimed invention must be found in a single prior art reference, arranged as in the claim." *Brown v. 3M*, 265 F.3d at 1360. Accordingly, it is believed that STILL does not constitute an anticipation of the presently claimed invention. Reconsideration and withdrawal of the Section 102 rejections are respectfully requested.

Even if, arguendo, the Office Action does not impermissibly combine elements from different embodiment, STILL cannot anticipate claim 27 or any claim depending therefrom because it does not disclose each and every feature of the claim. See MPEP § 2131.

The present invention, as presently claimed, is directed to a system for obtaining an image of the location(s) of one or more signals indicative of the presence of one or more substances to be detected, which substances are located at different positions relative to one another. This system includes a "sensor layer", which is a sheet of diffusion-controlling matrix material which contains one or more biological sensor materials (bioluminescent cells with reporter gene constructs) suspended throughout. It also includes appropriate means for detecting the location of the signals produced by the sensor material in response to the presence of substance(s) to be detected. In operation, substance(s) to be detected is/are brought into contact with the sensor layer at discrete locations. The substance(s) then diffuse into the sensor layer

and contact the bioluminescent cells with reporter gene constructs which in turn produce signals. These signals are finally detected, thereby providing the locations in the sensor layer which are in contact with the substance(s) to be detected. Moreover, as set forth above, independent claim 27 also recites a system for obtaining a spatially-resolved image of signals indicative of the presence of at least one substance, where the signals are produced by "bioluminescent cells with reporter gene constructs."

It is Applicants' view that STILL does not anticipate the presently claimed invention because, *inter alia*, STILL does not teach or suggest a sheet of diffusion-controlling matrix comprising a biological sensor material formed from bioluminescent cells with reporter gene constructs. Bioluminescence, according to Applicants, differs in principle from the signal-generating methods of STILL. For example, the detection of bioluminescence involves different technologies compared with the detection of color changes or fluorescence properties of the cells found in STILL. At best, STILL relates to the detection of cells by extracellular signals generated by fluorescence-activated compounds. Any cells used by STILL require additional substrates (e.g. vital dyes, precursors of fluorescent dyes) to be placed into contact with the cells as a necessary component for signal production. Such signals are generated by secondary extracellular processes, i.e. where the signal-generating dye or substrate must be acted upon outside the cell for there to be a detection. Such extracellular signal generation can lead to more diffuse, less spatially-defined images. This contrasts with the present invention, as the bioluminescent cells effectively function as point light sources, which facilitates obtaining a well-resolved spatial distribution of bioactivity in response to the compounds being tested, and in turn, better detection of useful compounds.

For at least the foregoing reasons, independent claim 27, and all claims depending therefrom, define subject matter that is not anticipated by STILL. Reconsideration and withdrawal of the rejection applied to claims 27-29 and 31-36 under 35 U.S.C. §102(b) are respectfully requested.

III. Rejections under 35 U.S.C. § 103 are overcome

The Office Action rejected claims 37, 38-39, 40, and 41-43 under 37 C.F.R. § 103 as allegedly being obvious over STILL in view of Simpson et al. (U.S. Patent No. 6,117,643) ("SIMPSON"). The Office Action further rejected claim 30 under 37 C.F.R. § 103 as allegedly being obvious over STILL in view of Ribi et al. (U.S. Patent No. 5,156,810) ("RIBI"). Applicants respectfully disagree with these rejections and traverse the rejections, taken together, as follows.

It is respectfully pointed out that "[t]o establish *prima facie* obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art." *See In re Royka*, 490 F.2d 981, 180 (CCPA 1974) and M.P.E.P. § 2143.03. Further, "[i]f an independent claim is nonobvious under 35 U.S.C. 103, then any claim depending therefrom is nonobvious." *See In re Fine,* 837 F.2d 1071 (Fed. Cir. 1988). Here, it will be shown that none of the rejected claims are obvious over the asserted combinations of references as none of the references, either taken separately or together, teach or fairly suggest each and every limitation of the claims.

The Office Action separately combines STILL with SIMPSON or RIBI to allege in each case a *prima facie* case of obviousness. As pointed out above, however, STILL does not anticipate the present invention, in particular, independent claim 27, as it does not teach or suggest each and every element of the presently claimed invention.

Neither SIMPSON nor RIBI cure the deficiencies of STILL. SIMPSON relates generally to micro-luminometer system comprising a bioreporter and an integrated circuit that detects the concentration of a select substance. SIMPSON is cited for its alleged teachings relating to the subject matter of dependent claims 37, 38-39, 40 and 41-43. RIBI generally relates to biosensors for detecting analytes on the basis of changes in the properties of a polymeric electrically conducting layer in response to an analyte. RIBI is cited for its alleged teachings relating to the subject matter of dependent claim 30. Neither SIMPSON nor RIBI teach, alone or in combination with each other or with STILL, a system for obtaining a spatially-resolved image of signals indicative of the presence of at least one substance, comprising (a) a sheet of diffusion-controlling matrix of dimensions sufficient to permit bringing material to be detected into contact

with at least one spatially-discrete area of said sheet, said matrix being selected from the group consisting of secondary valence gels, synthetic polymer gels and viscous solutions; (b) at least one biological sensor material suspended throughout said sheet of diffusion-controlling matrix and capable of producing at least one signal in response to the presence of at least one substance which is in contact with at least one spatially-discrete area of said sheet of diffusion-controlling matrix, said at least one biological sensor material being bioluminescent cells with reporter gene constructs, and (c) means for detecting the spatial distribution, relative to said sheet of diffusion-controlling matrix, of signal(s) produced in said sheet of diffusion-controlling matrix by said biological sensor material when said at least one substance is in contact with at least one spatially-discrete area of said sheet of diffusion-controlling matrix.

As none of the cited prior art, either alone or in combination, render independent claim 27 *prima facie* obvious, it follows that the rejected dependent claims are, by extension, nonobvious over the cited combinations of references. In other words, none of the deficiencies of STILL are cured in any way by SIMPSON or RIBI and thus, none of the reference combinations meet the legal standard to render the claims obvious.

Accordingly, reconsideration and withdrawal of the rejection under Section 103 are respectfully requested.

CONCLUSION

It is respectfully submitted that all of the claims now pending in the subject application are directed to patentable subject matter and allowance thereof is earnestly solicited.

Applicant submits that this Request for Reconsideration does not raise new issues for consideration nor necessitate the undertaking of any additional search of the art by the examiner, and thus may be properly entered into the record.

The Director is hereby authorized to charge any deficiency in the fees filed, asserted to be filed or which should have been filed herewith to Deposit Account No. 04-1105.

Respectfully submitted,

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